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**ENVIRONMENT DIRECTORATE**
**JOINT MEETING OF THE CHEMICALS COMMITTEE AND THE WORKING PARTY ON CHEMICALS, PESTICIDES AND BIOTECHNOLOGY**

**Cancels & replaces the same document of 19 September 2017**

## Test Guidelines Programme

# 10TH MEETING OF THE EXTENDED ADVISORY GROUP ON MOLECULAR SCREENING AND TOXICOGENOMICS

**Summary record**

**14-15 June 2017**

**OECD Conference Centre, 2 rue André-Pascal, 75775 Paris Cédex 16- France**

Nathalie Delrue

**JT03418964**

# SUMMARY RECORD

## 1. Opening

1. The tenth meeting of the Extended Advisory Group on Molecular Screening and Toxicogenomics (EAGMST) was opened by Bob Kavlock (United States , US ) and Maurice Whelan (European Commission, EC), co -Chairs of the EAGMST. The list of participants is included in Annex 1.

2. The main objectives of the meeting were to: 1) discuss candidate AOPs with respect to their readiness for external review ; 2) review and approve new project proposals for the EAGMST work plan ; 3) review the status and progress made in the development of the AOP Knowledge Base modules; 4) in addition, during the meeting, a session was dedicated to the discussio n of potential projects related to various 'omics techniques, especially transcriptomics, metabolomics and proteomics, with the objective to develop proposals that would delineate the scope of future EAGMST activities in this field.

## 2. Draft agenda

3. The draft agenda was approved without change [ENV/JM/TG/A(2017)4].

## 3. Report from the Secretariat

4. The Secretariat informed the group of the following recent outcomes:

- The new Series on Adverse Outcome Pathways was launched in September 2016 and is publicly available from the OECD i -library. AOPs are published there when they have been through the whole cycle of review and endorsement process.
- The Working Group of the National Coordinators for the Test Guidelines programme (WNT) at its meeting in April 2017 , approved the updated Guidance Document on Developing and Assessing Adverse Outcome Pathways without further modifications. This second edition of the Guidance Document is meant to

separate the practical guidance now contained in the Users' Handbook from the more generic and permanent guidance that is presented in the GD second edition.

- At its meeting in May 2017, the Joint Meeting (JM) strongly supported the AOP programme. This recognition at the policy level was welcomed by EAGMST. The JM also had a focus session on reconciling Integrated Approaches to Testing and Assessment (IATA) and Mutual Acceptance of Data ( MAD) and supported the development of Defined Approaches to testing and assessment (which consist of a fixed data interpretation procedure used to interpret data generated with a defined set of information sources) as components of an IATA that can be harmonised.
- The meeting of the Working Party on Hazard Assessment (WPHA, formerly th e Task Force on Hazard Assessment ) was held back-to-back with the EAGMST meeting. The EAGMST was updated on the status of the WPHA activities on IATA and the related case-studies project. The organi sation of an Information Exchange Webinar for IATA Related Projects was announced. At its meeting, the WPHA expressed interest in taking part in the AOP review process, especially at the level of the nomination of experts. The WPHA approved the inclusion on its workplan of 2 new projects, one led by Canada and EC HA on Guiding Principles for Establishing Weight of Evidence for Chemical Assessment ; one led by EC - Joint Research Centre and the US EPA on Development of Guidance for PBK models. Th e latter is also of relevan ce to EAGMST and was identified as a common project to be undertaken by EAGMST and WPHA (see para 55).

## 4. Perspectives from PAN Europe

5. A representative from PAN Europe presented the report published by PAN Europe in December 2016, titled "AOP The Trojan Horse for Industry Lobby Tools". In addition, several questions had been formulated by PAN Europe in advance of the meeting and were discussed by the group.

6. One particular concern raised by PAN Europe about AOPs was the potential oversimplification and misuse of AOPs in regulatory chemical safety assessm ent, which would lower the level of protection for humans and the environment from potentially hazardous chemicals. It was mentioned by PAN Europe that cases of direct use of AOP for Risk Assessment (RA) have been reported.

7. Oversimplification is also a co ncern shared by the group, but i t was clarified that AOPs cannot be applied to R A directly per s e since the mechanistic knowledge they convey needs to be somehow translated and incorporated into some RA strategy . There are many elements and steps in a RA and AOPs can inform some of these. Although the EAGMST can't control potential misuse, the group feels a responsibility to help avoid it by making every effort to provide supporting information and guidance to stakeholders that communicate clearly the key p rinciples and features of the AOP framework, including limitations and uncertainties . The WPHA has also an important role to play here too since it is taking the lead with regard to IATA and the application of AOPs in a RA context.

8. The review process of A OPs was explained (and is available from the document on lessons learnt). It was acknowledged that the quality, integrity and credibility of the AOP review process is of fundamental importance to the overall AOP programme and thus EAGMST intends to continu e to maintain high standards while looking for ways to keep things efficient. It was clarified that the name of the reviewers during the various steps is publicly available while th is is not the case in the context of a journal peer review. To improve comm unication to stakeholders, the Secretariat has developed a brochure on AOPs which was available for comments.

9. The group agreed that it i s still very early to suggest that IATA based on AOPs can be used to replace higher-tier *in vivo* testing although AOP -informed alternative testing strategies may provide very useful and complementary information, for example to better target *in vivo* testing, elucidate mode-of-action and potentially reduce the amount of animal tests required. It was acknowledged that the recent successes regarding non-animal IATA (inc. Defined Approaches) for assessing skin sensitisation were due in part to the availability of an AOP but were also very much due to the substantial research and development activities conducted internationally over many years.

10. The group confirmed that AOP development can potentially aid in identifying knowledge gaps in current risk assessment practice which in turn can target research priorities and inform test method development. The development of the AOP -KB is still in the early stages however and the brea dth of toxicology space is still quite limited and thus expectations need to be realistic and properly managed.

11. The group agreed that the re was a lot of commonality between open issues discussed under various agenda items of the EAGMST meeting and the points raised by PAN Europe . It was agreed that a very useful way forward, in the interests of good communication and transparency, would be to update the F requently Asked Questions (FAQ, see para 30) to reflect current thinking and state-of-the-art. The training sub-group will continue to lead these efforts and the agreement of PAN Europe to contribute was very much welcomed. Newly drafted FAQs can be circulated within EAGMST on more challenging issues so tha t members have the opportunity to share their views and contribute where they can.

# 5. External review

## 5.1. Outcome of external review

12. Two AOPs were subject to external review in March -April 2017, AOP 3 (Inhibition of the mitochondrial complex I of nigr o-striatal neurons leads to parkinsonian motor deficits ) and 12 (Chronic binding of antagonist to N -methyl-D-aspartate receptors (NMDARs) during brain development leads to neurodegeneration with impairment in learning and memory in aging). Due to the short time given to EAGMST to review the external review reports for AOPs 3 and 12, which were still draft documents, EAGMST approval was not requested at the meeting.

13. The scientific quality and strong weight of evidence ( WoE) of these AOPs was highlighted, although the v ery limited number of AOP stressors for these 2 AOPs was underlined. The constructive discussion between external reviewers and the authors at the end of the external review was acknowledged.

14. The question of the re -use of an existing KE R was common to the se 2 AOPs. Although the sharing of KER in AOP development is encouraged, it may cause confusion for the reviewers when a stressor comes from a shared KE R and has not been introduced in the AOP (e .g. paraquat in AOP 3). In addition , best practices applying to the revision of shared KEs or KERs may need to be established since authors sometimes feel reluctant to take on board revisions suggested by reviewers when they concern a KE or KER for which they don't have the ownership. The recommendation from EAGMST was that it may be useful for authors to discuss with the original author of a shared KE or KER in order to solve an issue. The key question is transparency. Anything can be revised but it needs to be transparent. Development of working instruction s in the future to guide that process was recommended. The training group was requested to help with this issue.

15. Over the summer, the AOP authors will finalise the revision of their AOPs, as necessary, based on the comments received. When ready, the Secretariat will circulate the 2 revised AOPs and the corresponding external review reports to the EAGMST by written procedure, asking for approval and subsequent release to WNT and WPHA for endorsement.

16. The 3rd AOP was briefly discussed, AOP 23 Androgen receptor agon ism leading to reproductive dysfunction. This AOP was reviewed last year and discussed at the last EAGMST meeting. This AOP has now been revised to reflect the external review comments. It was agreed that unless the Secretariat receives any comments on th e revisions made, this AOP would be sent to the WNT and WPHA together with AOP 3 and 12, as a package.

## 5.2. Review process

17. Although not many AOPs were submitted to external review this year, more and more AOPs are now ready to enter the review process. Eight AOPs were submitted for internal review in early 2017 and before completion of th e process, a new batch of 6 AOPs was ready for internal review. In the context of this strong review demand, the group discussed how to expedite the review process and examined several options.

- Sean Hays (US), president of SciPinion, was invited to present the opportunities offered by SciPinion, a company that organises outsourced peer review s. The group however expressed concerns that in this model the reviewers are typically paid. Moreover, the prospect of having AOP developers paying for the review of their own AOP would be highly undesirable.
- In the current process, as designed by EAGMST a t the start of the 1st reviewing process, reviewers are not paid but the external review requires the recruitment of a review manager who is paid . While th e financial burden is currently on the OECD Secretariat, it could shift to member countries who were asked if they could sponsor AOP reviews, not necessary from their country . This propo sal is developed at the end of the lessons learnt document i.e. "Sustainability of the external review", as one possible means to share the burden and expedite the review process.

18. It was agreed that based on the document on lessons learnt, the Secretariat would develop a kind of Standard Operating Procedure (SOP) for AOP review; this document would formalise the review process so that 3rd parties could take it over while ensuring consistency and reliability.

19. Representatives from the Endocrine Society offe red to use the Endocrine Society as a means of carrying out an external review. Essentially, peer-reviewers engaged by the Society's scientific journals could be requested by the Society (e.g. via journal editors) to act as external reviewers for selected AOPs related to endocrine-related effects . This proposal, which could lead to an attractive way to perform external reviews, received full support from EAGMST and it was indicated that other societies could be contacted in the future for other, non -endocrine related AOPs. The SOP for AOP review will be very useful in this respect. The Endocrine Society will contact journal editors and will work with the Secretariat to organise the external review of one or two endocrine related AOPs.

## 6. Outcome of the Internal review and readiness of AOPs for external review

20. The following AOPs were reviewed during the 1st quarter of 2017 and subsequently revised by their authors . The outcome of the internal review was presented by the internal reviewers and discussed by the gr oup. The group acknowledged the work done as well as the high quality of the AOPs in general which very much conform to the Users' Handbook. The quality of the internal reviews was also highly appreciated.

- AOP 202: In utero DNA topoisomerase II inhibition leading to infant leukaemia

As mentioned during the discussion on external review (item 5), it was recognised that establishing the weight of evidence based on one stressor only becomes a challenge.

The authors agreed to the reviewers' recommendation to include double strand break as an additional Key Event.

The reviewers also recommended to make clear from the beginning of the AOP that the MIE happens in utero but to keep the MIE general, so that it can be re-used if needed, not only in utero. However, different views were expressed; some experts were of the opinion that it is important to keep the life stage specificity of the MIE, especially, as noted by the authors, because infant leukaemia is a cancer with in utero origin, which needs to stay very clear in the AOP.

Conclusion: The AOP was considered good to go to external review following necessary revision and final look from the internal reviewers.

- AOP 10: Binding to the picrotoxin site of ionotropic GABA receptors leading to epileptic seizures

Redundancy and duplication of content between some KE and KER descriptions were reported by the reviewers and it was noted that this could be addressed by providing more guidance in the revised version of the Users' Handbook.

This AOP includes a quantit ative WoE table. The inclusion of this pilot table was welcome provided the values are transparent and the table is consistent with the Users' Handbook. More work may be needed to ensure compatibility with the Users' Handbook, e.g. provide more the rationale, add additional background.

Conclusion: The EAGMST d elegated the responsibility to give the green light for external review to the Handbook group and the internal reviewers.

- AOP 54: Inhibition of Na+/I - symporter (NIS) decreases TH synthesis leading to learning and memory deficits in children

The issue of shared KER/KE was raised again since the reviewers recommended revising a KER ( Decreased, Thyroid hormone synthesis leads to Decreased, Thyroxin (T4) in serum) and the AO which are currently not in l ine with the Users' Handbook, while the authors indicated that this cannot be done (see also para 1 4) since these KER/AO have been developed by other authors and published already.

The recommendation from EAGMST was that it may be useful to discuss with t he original author of this event in order to solve this issue (see also para 1 4). An alternative option was to create another AO, but this was not recommended.

Conclusion: The authors will go back to the internal reviewers when this issue is solved before moving forward to external review.

- AOP 131: AhR activation leading to uroporphyria

Conclusion: This AOP was recommended for the external review by the internal reviewers and confirmed by the EAGMST.

- AOP 150: Aryl hydrocarbon receptor activation leading to embryolethality via cardiotoxicity

and

- AOP 21: AhR activation leading to embryo toxicity

Conclusion: The EAGMST suggested that since they have a common basis, these two AOPs should be reviewed together in parallel by the same external reviewers if they progress at the same way.

Before they go to external review, the authors of these two AOPs need to get together and make sure they respond in a consistent way to the comments from the internal review.

- AOP 154: AOP on binding of FK506 -binding protein 12 (FKBP12) by calcineurin inhibitors leading to immunosuppression

Conclusion: This AOP was not considered ready for external review. In particular, the supporting evidence was considered incomplete and WoE analysis and overall assessment of the AOP not sufficient.

- AOP 6: Antagonist binding to PPARalpha leading to starvation-like body-weight loss

The internal reviewers suggested that several KEs could be combined, however, the authors strongly felt that they are separate events and need to be kept separate. Reviewers and the author would need further discussion to solve this issue and some general guidance potentially derived on the branching approach.

Conclusion: the AOP remains open to external review but more work on resolving the issues is first needed.

- AOP 42: Inhibition of Thyroperoxidase and Subsequent Adverse Neurodevelopmental Outcomes in Mammals

Conclusion: the AOP was considered good to go to external review following a few more revisions from the authors and final look from the internal reviewers.

21. The external review will start later in 2017, once further work that has been identified has been completed and AOPs get the green light from the internal reviewers. The Secretariat will get back to the authors after the meeting and discuss timelines.

# 7. Proposed Updates to the Users' Handbook

## 7.1. Users' Handbook updates

22. The Revised Users' Handbook was circulated by the Secretariat to EAGMST for written comments by 30 June 2017. The meeting was the opportunity to present the major revisions made including: guidance on how to handle branching in an AOP ; new text to describe how to depict feedforward/feedback loops ; new guidance on assigning calls for applicability terms for KE(R)s ; additional guidance on defining applicability domains ; elimination of direct and indirect relationship terminology.

23. Japan requested that the Users ' Handbook (i) include information about the process for AOP submission at OECD and (ii) recommended that project submitters consult their member country and get support from them before submission. Additional comments received from EAGMST by 30 June will also be taken into consideration in the preparation of the next draft.

24. Following repeated discussions after the last EAGMST meeting on how inflammation could be represented in AOPs to facilitate network-building, a two-day workshop will be organised by the JRC in September to bring experts in inflammation-mediated toxicity together to discuss and identify salient and indicative events in inflammogenesis and to find best ways for representing the inflammatory process in the context of AOP development and application.

25. In addition, it was mentioned as a general recommendation for the Wiki team that the quality of the snapshots would need to be improved so that the resolution of the figures is as good as the one in the Wiki.

### 7.2. Outcome of SETAC Pellston Workshop - WG1 & WG2

26. Dan Villeneuve and Ed Perkins presented the outcome of 2 Work Groups (WG) at the SETAC Pellston Workshop on Advancing the Adverse Outcome Pathway Concept – An International Horizon Scanning Approach (April 2017, Canada); respectively WG 1 on AOP Networks and WG 2 on quantitative AOPs and their applications. The manuscripts from the Pellston Workshop will be published in the coming months.

## 8. Report from the training group

27. The training group updated the EAGMST on the recent and upcoming training activities. Many training session are organised for various audiences and in various regions of the world. An online AOP e-course has also been developed on the initiative of the Human Toxicology Project Consortium and covering the AOP concept, program and the AOP-KB.

28. It was suggested that some sort of certification process could be developed to be associated with certain training courses. This could be desirable, for example, to bring some guarantee that new developers have sufficient knowledge of the Users' Handbook and guidance before they start an AOP.

29. The group expressed concerns that a certification system would restrict the development of AOPs. The group was more in favour of sending a strong incentive to e.g. new AOP developers to take the course, but not necessarily receive a certificate. It was agreed not to use the term certification, but instead have something like a quiz embedded in the course as a way of reinforcing the learning experience and providing an informal means of self-assessment. A number of such examples were mentioned, for example in relation to online safety training courses.

30. The Frequently Asked Questions (FAQs) developed by the training group were sent for comments to the EAGMST before the meeting. They were based on a recent global scanning exercise. This current list of FAQs was mainly developed for AOP developers but other questions may be developed for other audiences, depending on the

needs. PAN Europe and Endocrine Society expressed the wish to bring additional questions to the FAQs (see para 11).

31. The EAGMST suggested one way to broaden the engagement of the stakeholder community could be to target formal education. The training team could prepa re slides for university teachers. It would help students be aware of the AOP P rogramme and may be have them contribute e.g. development o f AOPs within the context of a research project or thesis.

32. It was agreed that more emphasis should be given to develo p a training approach and materials to more effectively inform the non-scientific stakeholders and in particular, those in positions of power and influence (l eaders, managers, policy makers etc.). Here the emphasis needs to be more on the relevance and ultimate utility of the AOP framework in supporting decision making (i.e. the 'why') and less on more technical aspects such as AOP development (i.e. the 'how').

# 9. Work plan of the AOP development Programme

## 9.1. New projects

33. Two new project proposals were submitted and discussed:

- PPARγ inactivation leading to lung fibrosis (Korea)

It was noted that this AOP has interlinks with some KEs in AOP 38 on Protein Alkylation leading to Liver Fibrosis . Some of these KEs are not organ specific so could be reused. Links can also be made with AOP 173: Secretion of inflammatory cytokines leading to lung fibrosis. It was recommended that the developer of this new AOP (Jinhee Choi) consult the authors of AOP 173 ( Sabina Halappanavar ) and AOP 38 (Brigitte Landesmann) in the course of the development of the AOP.

- Secretion of inflammatory cytokines after cellular sensing of the stressor leading to plaque progression (Denmark)

34. Both proposals were approved and included in the AOP development workplan.

## 9.2. Workplan – general

35. It was pr oposed to migrate the AOPs from project 1.29 ( Putative AOPs) to the SAAOP category, while AOPs in this category when they are sufficiently advanced would be submitted as a separate OECD project.

36. The authors will be contacted by the Secretariat after the m eeting and invited to provide updates of their respective projects. The AOP workplan will be revised after the meeting, with the inclusion of the new projects approved during the meeting and updates from the existing ones.

## 10. AOP application: from case studies to regulatory application

37. The group discussed how to strengthen the links with WPHA and the WNT and work towards an enhanced application of AOPs. It was reported that at its meeting, the WPHA identified the need to more closely relate AOPs to regulatory endpoints, in order to serve the need of the assessors.

- The WNT Standard Project Submission Form (SPS F) template will include an optional section inviting the submitter of an SPSF to consider the related AOPs available in the AOP KB, in order to identify potential gaps that could be brought to the attention of EAGMST as a priority for AOP development. The objective is that expert groups consider the relevant AOPs in their field of expertise and go to the EAGMST with suggestions for orientated AOP development.
- Project for an IATA on non-genotoxic carcinogens (NGTxC) – in the context of this project, case studies will be conducted, based on AOPs and exploring how to combine relevant *in silico* and *in vitro* assays.
- The outcome of the discussions at the SETAC Pellston WG3 on regulatory use of the AOP framework and the perspective of the US on Establishing New Approaches for Evaluating the Safety of Chemicals and Medical Products in the United States were presented.

## 11. Special session on 'omics': transcriptomics, metabolomics and proteomics

38. Following previous discussion s at the EAGMST meeting in 2016, a special session on 'omics was organised this year, with the objective to develop proposals that would delineate the scope of future EAGMST activities in this field . Several presentations on transcriptomics, metabolomics and proteomics were made in order to set the scene, discuss the roadblocks for use of 'omics data in a regulatory context, and how this group or others at OECD could contribute to a better use of the data generated.

39. A r eport from an ECETOC workshop in October 2016 indicated that methodological uncertainties in the generation, storage, processing, and interpretation of 'omics data limit their application in regulatory toxicology . Other roadblocks were al so identified such as the lack of best practice guidelines, the lack of training opportunities, the lack of relevant and appropriately designed case studies that address a regulatory purpose. Omics techniques however, are now considered mature enough (espe cially transcriptomics and metabolomics) and could contribute to e.g. identification of molecular Key Events, accelerat ion of AOP development, grouping and read -across, or weight-of-evidence based hazard assessment within IATAs.

40. A reporting framework for t he 3 omics approaches was thus identified as something that is missing, and which would induce reproducibility and help regulatory acceptance. Availability of reference material would allow intercomparison in order to progress towards data interpretation. It was acknowledged that although the development of such framework is not sufficient, it is essential and is seen as a 1st step towards using 'omics data in regulatory toxicology.

41. The project proposal initiated by the UK and now also supported by Canada o n the Construction of a series of guidance documents for consistent treatment and reporting of 'omics data from various sources was supported by EAGMST, as well as having an EAGMST sub-group working on the project.

42. Tim Gant, Jason O'Bri en, Carole Yauk, Ru sty Thomas, Mark Viant, Ed Perkins expressed interest in joining the project leading team. Expertise outside EAGMST will be sought too. It will be up to this group to delineate more concretely the scope of the project. It was agreed that the current projec t description would be revised to reflect the outcome of the session at the meeting . It would then be circulated and discussed for formal inclusion in the EAGMST workplan at the December TC.

43. The group also discussed h ow to use omics more effectively in AO P development, and the demonstration of the application of 'omics in case studies.

## 12. Updates on the AOP-KB

44. The Adverse Outcome Pathway -Knowledge Base (AOP -KB) is currently implemented as a federated system consisting of individual modules (currently, the AOP-Wiki and Effectopedia) that serve unique roles within the knowledgebase , and a portal that provides access to information from all the individual modules.

45. In May 2017, the AOP -KB development team agreed that the best path forward was to phase out the cur rent federated system and move toward a centralised knowledgebase to house all content. The AOP-KB presented this project to the EAGMST and explained that this would avoid issues related to synchronisation of the 2 modules (Wiki and Effectopedia) , would be less resource consuming and would avoid any potential confusion among users in relation to which of the 2 modules should be used. AOP developers were reassured that while moving from the current AOP KB 1.0 to the new AOP-KB 2.0, all the data will be transferred smoothly. People can continue working with the Wiki, which will be maintained until AOP KB 2.0 is ready and everything will then be transferred.

46. It was noted that since the user interface will change, the Users ' Handbook will need to be adapted. The Users' Handbook drafting team will take care of this update.

47. In the future, the SAAOP will thus stop maintaining the Wiki but will continue to oversee non-OECD AOPs, manage gardening activities and assist newcomers.

48. A technical update was provided for the various AOP KB modules:

- Intermediate Effects Database – IEDB: it is expected to be launched in 2018, pending an ongoing review of the OECD Harmonized Template 201, which is the basis for capturing the information for this module.
- e.AOP.Portal: represents the main entry point for the AOP -KB. It is a search engine for all AOPs and KEs and allows browsing of external review reports for individual AOPs. It was suggested that information could be searched by key terms, which could be envisioned when ontology is better established.
- AOP Wiki: the release of a new version, AOP -Wiki 2.2 is tentatively planned for September 2017. Major efforts have been made with ontologies, although one encompassing all ontologies is very difficult to achieve. AOP -Wiki 2.2 will include the following functionalities:
  - AOP-XML export option
  - Synchronization with updated OECD handbook
  - Additional usability features based on user feedback
  - Incorporate network views from AOPXplorer
- AOPXplorer: set to launch in 2017 and is currently availa ble for beta testing. It provides a network views for the AOPs.
- An XML standard has been defined to describe the minimal data exchange format for the AOP-KB modules. This standard for data exchange between the AOP -KB modules is fully compatible with the A OP extended Ontology. The schema is finalised and is ready for release. AOP -Wiki data were successfully exported as AOP-XML and were imported into Effectopedia.
- Effectopedia: the release of Effectopedia beta version 1.0 at the end of 2016 was followed by the development of training materials. Bugs were fixed and a proof of concept web application is expected for the summer 2017. The team involved in the development of Effectopedia has increased a lot since 2016.

49. Going back to the AOP-KB user needs survey conducted in July 2015 , it was acknowledged that a lot of the high and medium priorities identified 2 years ago have been accomplished or are on track. One objective for the future is to be able to cost the development and maintenance of the AOP-KB more fully in order to help secure funding and attract reasonable medium-term to long-term funding sources. A new user needs on-line survey will be launched in September. A dedicated conference call of EAGMST may be organised to discuss the responses and the AOP-KB development plans.

50. The EAGMST officially endorsed the proposal from the AOP KB team to go for the AOP-KB 2.0. The AOP KB team was asked to draft a way forward document in order to describe how this will be conducted. It is expected that this project proposal will be circulated to the EAGMST in the autumn and then included in the workplan at the EAGMST December Teleconference. It was indicated that contribution to the project is welcome and the Secretariat is looking forward to recruiting new sponsori ng Member States or entities.

## 13. Strategic development of the AOP program

51. The following priorities for EAGMST were identified:

- Put the AOP Programme on a stable and sustainable footing (5-year horizon)
- Include other relevant topics within the work plan (e. g. ADME/TK, 'omics, HTS/HCS, …)
- Strengthen cooperation with key OECD groups (e.g. WPHA, WNT, …)
- Increase outreach and engagement within OECD member countries . E AGMST delegates in particular were invited to work as ambassadors and contact points of the acti vities of this group in their countries and commit to the goal of reaching out to relevant actors and initiatives in their country.

52. It was also indicated that the WG 4 at the SETAC Pellston Workshop recommended the development of a r oadmap to expand aware ness of, involvement in, and application of the AOP framework and AOP knowledgebase in the broader scientific and regulatory/environmental policy communities . This roadmap would include the following elements (to be captured in a peer-review paper in the coming months):

- Publishing, deposit and review strategy (e.g. develop partnerships with journals, in addition to AOP KB)
- Education and training (as developed by the training team)
- Increase Stakeholder-specific interactions
- Translation of knowledge into ap plication (including c o-development of case studies with stakeholders, monitoring uses and potential misuses)
- Governance and sustainability (go beyond SAAOP; consider SETAC and SOT involvement; d efine a business plan to attract potential investors ; l ook to international funding programmes)
- Development of indicators of impact of AOP framework

53. The outcome of a n International Workshop hosted by the US EPA in September 14-15, 2016 in Washington DC, on Accelerating the Pace of Chemical Risk Assessments was pres ented. The objective of the workshop was to discuss the advent of new alternative methods (NAMs) for generating safety information on chemicals. As an outcome, case study proposals are being drafted, and will ultimately be conducted by multinational groups, including OECD following the workshop.

54. There was clear s upport from the EAGMST for the development of regulatory application case studies, brought by participants, included in the EAGMST workplan, reviewed by EAGMST; and work on together with WPHA. This would also be supported from the perspective of the WPHA since there is a lot of interest in how AOP can be used to inform risk assessment. The submission of case studies was encouraged.

## 14. Project proposals in the Biokinetics area

55. Maurice Whelan introduced 2 proposals:

- Proposal for the development of a Guidance document on the characterisation, validation and reporting of Physiologically Based Kinetic (PBK) models for regulatory applications

This proposal, led by EC - Joint R esearch Centre and the US EPA includes 3 main aspects, (i) model characterisation, (ii) model validation and (iii) model reporting. The project proposal was included in the workplan of the WPHA at its meeting. The EAGMST also agreed to include it in its workplan as a project to be deve loped in collaboration with the WPHA.

France expressed interest in getting involved in this project. Interested people are welcome to join the group in charge of drafting the guidance.

- Proposal for development of a Biokinetics Knowledge Base

A very preli minary outline proposal was presented to stimulate thought and discussion. The main idea is to consider the development of a knowledgebase to optimally capture and integrate (mechanistic) knowledge underpinning biokinetic (toxicokinetic) processes (adsorption, distribution, metabolism, excretion), much like the AOP -KB captures knowledge specific toxicodynamic processes. Considering the importance of biokinetic information within an IATA context, it seems logical to give equal attention to managing and explo iting biokinetics knowledge by adopting an overall approach that is similar to the AOP framework. Members are invited to contact EC -JRC if they are interested in exploring this avenue.

## 15. Any Other Business and Conclusions by the Chairs

### 15.1. Advancing Adverse Outcome Pathway (AOP) Development for Nanomaterial Risk Assessment and Categorisation: Progress Report

56. The EAGMST was informed that a t the last meeting of the Working Party on Manufactured Nanomaterial (WPMN), it was agreed that an information sharing se ssion (e.g. by WebEx) between WPMN expert group on AOPs and the EAGMST training group would be organised in the future, in order to ensure coordination between the EAGMST and the WPMN for the WPMN project on Advancing Adverse Outcome Pathway (AOP) Development for Nanomaterial Risk Assessment and Categorisation.

## 15.2. Dates for next year and potential common session with WHPA

57. The next EAGMST meeting will be held in Paris, on Thursday/Friday 28-29 June 2018. This meeting will be held back to back with the WPHA meeting (26-27 June 2018). The Secretariat will consider organising a joint session between the 2 groups , potentially in the afternoon on the 27th.

## Annex 1 - Participants List for 10th Meeting of the Extended Advisory Group on Molecular Screening and Toxicogenomics

### 1. Participants in face to face meeting

*Australia*

**Sneha SATYA**
*Head, Targeted Assessments Program*
*Department of Health*
*NICNAS*

*Belgium*

**Dries KNAPEN**
*Associate Professor*
*Veterinary Sciences*
*Universiteit Antwerpen Campus Drie Eiken*

**Mathieu VINKEN**
*Professor*
*In Vitro Toxicology and Dermato-cosmetology (FAFY)*
*Vrije Universiteit Brussel (VUB)*

*Canada*

**Jason O'BRIEN**
*Research Scientist - molecular ecotoxicology*
*Ecotoxicology and Wildlife Health Division*
*Environment and Climate Change Canada*

**Carole YAUK**
*Research Scientist, Genomics*
*Mechanistic Studies Division*
*Health Canada*

**Tara S. BARTON-MACLAREN**
*Sr. Manager, Assessment Methodology Divisions*
*Existing Substances Risk Assessment Bureau*
*Health Canada*

**Bette MEEK** *Associate Director, Chemical Risk Assessment*
*University of Ottawa*
*McLaughlin Institute for Population Health Risk Assessment*

*Denmark*

**Marianne DYBDAHL** *Senior Researcher*
*Division of Toxicology and Risk Assessment*
*National Food Institute*

*France*

**Emmanuel LEMAZURIER**
*INERIS - Direction des Risques Chroniques*

*Germany*

**Tanja BURGDORF**
*Federal Institute for Risk Assessment (BfR)*

**Stefan SCHOLZ**
*Department of Bioanalytical Ecotoxicology*
*Helmholtz Centre for Environmental Research GmbH – UFZ*

*Italy*

**Annamaria COLACCI**
*Chief*
*Environmental Toxicology and Risk Assessment*
*Environmental Protection and Health Prevention Agency*
*Emilia Romagna Region*

**Sabrina TAIT**
*LIFE PERSUADED Project Manager Collaborator*
*Center for Gender-Specific Medicine*
*National Institute of Health (ISS)*

**Olga TCHEREMENSKAIA**
*Environment and Health Department*
*Istituto Superiore di Sanita (ISS)*

*Japan*

**Hajime KOJIMA**
*Secretary General*
*Japanese Center for the Validation of Alternative Methods (JaCVAM),*
*Biological Safety Research Centre (BSRC)*
*National Institute of Health Sciences (NIHS)*

**Takashi YAMADA**
*Section Chief*
*Division of Risk Assessment, Biological Safety Research Center*
*National Institute of Health Sciences (NIHS)*

**Shihori TANABE**
*Senior Researcher*
*Division of Risk Assessment, Biological Safety Research Center*
*National Institute of Health Sciences (NIHS)*

**Tomoko AOYAGI**
*Chief*
*Safe Assessment Division, Chemical Management Center*
*National Institute of Technology and Evaluation (NITE)*

**Taisen IGUCHI**
*Professor*
*Yokohama City University*

**Fumiyo SAITO**
*Section Chief*
*Research Section 1, Research Department I, Chemicals Assessment and Research Center*
*Chemicals Evaluation and Research Institute (CERI)*

***Korea***

**Jinhee CHOI**
*University of Seoul*

**Kyungho CHOI**
*Professor*
*Seoul National University*

**Joohyon KIM**
*Senior researcher*
*National Institute of Environmental Research (NIER)*

**Sanga MOON**
*Researcher*

**Jung-Hwa OH**
*Pricinpal Research Scientist*
*Department of Predictive Toxicology*
*Korea Institute of Toxicology (KIT)*

**Seo Young YOON** *program officer*
*Ministry of Environment, Korea*

***Netherlands***

**Mirjam LUIJTEN**
*Centre for Health Protection*
*National Institute of Public Health and the Environment (RIVM)*

**Lidka MASLANKIEWICZ**
*Centre for Safety of Substances and Products*
*National Institute of Public Health and the Environment (RIVM)*

***Switzerland***

**Rex FITZGERALD**
*Regulatory Toxicology Expert*
*Swiss Centre for Applied Human Toxicology*
*University of Basel*

**Walter LICHTENSTEIGER**
*Professor*
*Group for Reproductive, Endocrine and Environmental Toxicology*
*GREEN Tox*

**Inge WERNER**
*Swiss Centre for Applied Ecotoxicology Eawag/EPFL*

***United Kingdom***

**Tim GANT**
*Professor*
*Toxicology*
*Public Heath England*

**Alan Jeffrey HARGREAVES**
*Reader*
*School of Science and Technology*
*Nottingham Trent University*

**Miriam JACOBS**
*Principal Toxicologist*
*Department of Toxicology*
*PHE*

**Emma MARCZYLO**
*Principal Toxicologist*
*Toxicology*
*Public Health England*

**Mark VIANT**
*School of Biosciences*
*University of Birmingham*

***United States***

**Lyle BURGOON**
*Toxicogenomic Informatics & Solutions, LLC*

**Robert KAVLOCK**
*Deputy Assistant Admin for Science*
*U.S. Environmental Protection Agency (EPA)*

**Edward J. PERKINS**
*Environmental Laboratory*
*U.S. Army Corps of Engineer*

**Russell THOMAS**
*Director*
*National Center for Computational Toxicology*
*U.S. Environmental Protection Agency*

**Daniel VILLENEUVE**
*Mid-Continent Ecology Division*
*U.S. Environmental Protection Agency*

***EU***

**Ahmed ABDELAZIZ**
*Managing Director*
*Rosettastein Consulting UG.*

**George FOTAKIS**
*Scientific Officer*
*ECHA*
*European Chemicals Agency (ECHA)*

**Brigitte LANDESMANN**
*European Commission Joint Research Centre*

**Maurice WHELAN**
*Head of Unit - Chemical Safety and Alternative Methods*
*Directorate for Health, Consumers and Reference Materials*
*European Commission Joint Research Centre*

**Clemens WITTWEHR**
*Health, Consumers & Reference Materials Directorate,*
*Chemical Safety and Alternative Methods Unit*
*European Commission Joint Research Centre*

***Business and Industry Advisory Committee (BIAC)***

**Richard CURRIE**
*Non-Governmental Delegate (NGD)*

**Shunji NAKAI**
*General Manager*
*Japan Chemical Industry Association (JCIA)*

**Gladys OUEDRAOGO**
*Scientific Officer*
*Department of predictive models and method development*
*L'Oréal Research & Innovation*

***Environmental NGO***

**Ms. Angeliki LYSSIMACHOU**
*Environmental Toxicologist*
*Pesticides Action Network Europe (PAN Europe)*

**Jean-Pierre BOURGUIGNON**
*Endocrine Society*

**Shirlee TAN**

*Endocrine Society*

***International Council on Animal Protection in OECD Programmes***

**Esther HAUGABROOKS**
*Toxicologist*
*Physicians Committee for Responsible Medicine*

**Catherine WILLETT**
*Director, Regulatary Toxicology, Risk Assessment and Alternatives*
*Regulatory Toxicology, Risk Assessment and Alternatives*
*Humane Society of the U.S./ Humane Society International*

***OECD***

**Hristo ALADJOV**
*Consultant*

**Patience BROWNE**
*Administrator, Test Guidelines*
*ENV/EHS*

**Sally DE MARCELLUS**
*Electronic Information Analyst*
*ENV/EHS*

**Nathalie DELRUE**
*Administrator, Test Guidelines*
*ENV/EHS*

**Bob DIDERICH**
*Head of Division*
*ENV/EHS*

**Anne GOURMELON**
*Principal Administrator, Test Guidelines*
*ENV/EHS*

**Eeva LEINALA**
*Principal administrator*
*ENV/EHS*

**Christina QUAGLIO**
*Assistant*
*ENV/EHS*

**Magdalini SACHANA**
*Administrator, Hazard Assessment*
*ENV/EHS*

*Other*

**Ksenia GROH**
*Food Packaging Forum Foundation*

**Julija FILIPOVSKA**
*Regulatory Toxicology & Policy Consultant*

## 2. Participants in the webinar

*Canada*

**Sabina HALAPPANAVAR**
*Research Scientist, Genomics Group*
*Mechanistic Studies Division*
*Health Canada*

*Denmark*

**Sarah Poulsen**
*Postdoc*
*National Research Centre for the Working Environment*

*United States*

**Warren CASEY**
*Director*
*NICEATM, NIEHS*

**Stephen EDWARDS**
*Systems Biologist*
*National Health and Environmental Effects Laboratory -*
*Integrated Systems Toxicology Division*
*U.S. Environmental Protection Agency*

**Suzanne FITZPATRICK**
*Senior Advisor for Toxicology*
*Center for Food Safety & Applied Nutrition / US Food and Drug Administration*
*DHHS/FDA/OC/OSHC*

**Mary GILBERT**
*Neurotoxicologist*
*Neurotoxicology Branch*
*US Environmental Protection Agency*

**Sean HAYS**
*President*
*SciPinion, LLC*

*EU*

**Andrea TERRON**
*Senior Toxicologist EUropean Food Safety Autority*
*Pesticide Unit*
*European Food Safety Authority (EFSA)*

***Business and Industry Advisory Committee (BIAC)***

**Katy GOYAK**
*Senior Toxicologist*
*Toxicology*
*ExxonMobil Biomedical Sciences, Inc.*